The patient was treated by betanaphtol and very constant sponging, and though the case proved a severe one, the temperature for the first week of her stay in the hospital being often in the neighborhood of 104° F. and the urine having to be drawn by catheter, she did well, and by the twenty-seventh day of the disease it was noted that the temperature was normal or subnormal, with the exception of a single rise to 100° F. Convalescence was looked upon as assured, when the child began to vomit, complained bitterly of pain in the abdomen, and the temperature quickly rose to 104° F. The pulse was 140. The question of perforation and peritonitis at once arose, as well as that of an appendicitis. But the high temperature and absence of collapse were against the former, and the fact that there was no tenderness or swelling in the right iliac fossa or at McBurney's point—indeed, that all the discomfort was at the upper part of the abdomen—set aside the latter. In the next few days the symptoms became more and more significant. The vomiting continued; at first curdled milk with bile-stained fluid, several ounces at a time, was ejected, then the same quantity of a pure, brownish, bilious fluid. Nothing was retained on the stomach—not even water—though a little later one-tenth of a grain doses of calomel stayed down, and small amounts of peptonized milk, and, still later, brandy and cracked ice; but the child had to be almost entirely nourished through the rectum, and sustained by hypodermatic injections of strychnine. There was some looseness of the bowels, and greenish stools were passed. The pain was very great, and she screamed with it; it was entirely referred to the upper part of the abdomen. Considerable tenderness over the region of the gall-bladder existed, and, on palpation, a tumor about the size of a lemon, and having the shape of the gall-bladder, could be felt and even seen through the abdominal walls; both recti muscles were very rigid, the right especially; the tenderness extended to the left hypochondrium.

Applications of ice did some good, but the great restlessness of the child caused them to be exchanged for hot fomentations, which she liked better. The conjunctivæ at first were not discolored, but they became increasingly so, until the jaundice was very perceptible; the urine contained bile-pigment, but no albumin. The temperature—which, soon after the beginning of the attack, marked 101° F., with pulse of 124 and respirations 24—reached 104° F. for a short time, but it soon subsided, and the thermometer indicated between 99° and 101° F., while the tumor and pain were manifest. In the course of the case the whole abdomen became tumid, and the tenderness as marked in the left hypochondrium as in the right. The spleen did not appear to be enlarged; there was no ascites. Abdominal pain, tenderness, and tumor gradually subsided, though even toward the end of the case occasional pain in the region of the gall-bladder recurred. The child became greatly emaciated during the attack, and showed in her face the severe illness through which she was passing. But a gradual recovery took place, and she was discharged from the hospital on March 31st in good condition.

In reviewing this case, the violence of the pain stands out as the most prominent symptom. I have never in any instance of typhoid fever seen it equalled, and the child often shrieked with it. There was no doubt in her mind of its seat; when questioned she always put her hand to the region under the ribs on the right side. The pain was aggravated by the incessant vomiting. In the other cases reported in this paper the jaundice was slight; here it was very marked. The gravity of the symptoms made me think of asking one of my surgical colleagues to perform an operation; but as, when I was considering the propriety of surgical interference, improvement began to show itself, this was deferred, and the child recovered without. From the absence of sweating and chills—though this is not conclusive—I believed the cholecystitis not to be purulent, which influenced my decision. On the whole, this is the most marked case of typhoid cholecystitis ending in recovery which I have met with. It is worthy of note that it occurred after convalescence had set in. Cholecystitis in typhoid fever is a complication generally arising in the third or fourth week of the fever. In one of the cases reported in this paper it came on in the relapse.

The treatment in the cases detailed consisted for the most part in the administration of fractional doses of calomel, frequently repeated, in combating the nausea, and in the local use of ice or of poultices. The former is to be tried first, and is, I believe, the more efficient. Counter-irritation, with turpentine stupes or with iodine, may also be used, and Case I. thought he derived much benefit from this. For the relief of the pain, hypodermatics of morphine may be necessary, and, as in Case III., the circulation may have to be supported by hypodermatics of strychnine and of digitalis.

THE INFLUENCE OF VARIOUS DIETS UPON THE ELIMINATION OF THE URINARY NITROGEN, UREA, URIC ACID, AND THE PURIN BASES.

(From the Pepper Laboratory of Clinical Medicine, University of Pennsylvania.
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SINCE the publication by Salkowski, in 1897, of his improved method for the estimation of the xanthin bases in the urine, we have been in the possession of a feasible and accurate procedure for the quantitative determination of these important substances. Simultaneously, the researches of Krüger and Salomon have given us reliable qualitative methods for the differential study of the individual members of the purin group. Thus we are now in a position to undertake comparative studies of the relations of these bases to various ages, states of health, diets, and diseases. We possess almost no accurate knowledge of the physiological or pathological relations of these bases. Nearly all the work already done has been carried through with the Krüger-Wulff method, whose unreliability, even for clinical work, has been conclusively demonstrated. Obviously, we need first of all physiological data, and it has been the purpose of these researches, whose partial results are herein reported, to furnish some such data.

I have believed it most advantageous, to the end of a perfect control of the studies, to submit myself to the diet experiments. Thus I was enabled to control specifically every detail of the studies, something which is impossible under other circumstances. My weight is about 160 pounds. My general health is perfect; my constitution is of the robust or plethoric type. The general plan of the studies has been as follows: The specific diet having been entered upon, the collection of the entire daily urine was begun upon the *third* day of the diet, and was continued for *six* successive days. The body-weight was noted before and after each period Between these periods of different diet a mixed diet was employed, except that tea, coffee, cocoa, chocolate, and alcoholic beverages were entirely avoided. I do not use tobacco. The only exercise taken was that involved in the laboratory work required for the estimations, which, together with other work, amounted in all to about seven hours of laboratory work daily. Seven hours of sleep, the normal personal quota, were taken daily. The total urinary nitrogen—the urea, the uric acid, and the purin bases—were estimated daily during the six days of each period; the total nitrogen was estimated by the Kjeldahl method; the urea by the Mörner-Sjöqvist method; the uric acid by the Salkowski-Ludwig method, as taught by Salkowski, and the purin bases by the new Salkowski method, for which I have only praise to utter. The total urine of the twenty-four hours was always diluted to 2000 c.c. (except when it naturally exceeded that volume), in order to have the determinations conducted under constant comparative conditions. For the estimation of the purin bodies, 1400 c.c. of this diluted urine were mixed with 350 c.c. of magnesia mixture and the phosphates removed by filtration; 350 c.c. of the filtrate were then used for the determination of the uric acid and 1125 c.c. for the bases; thus large quantites were used and the errors of manipulation correspondingly reduced. Since the method for the bases is not yet widely known, I will describe it in its main details: After the phosphates are removed from the urine by the magnesia mixture, the purin bodies, uric acid and the bases, are precipitated as silver-magnesia compounds on the addition of an excess of silver nitrate, and the precipitate kept out of solution by the strongly ammoniated reaction, which at the same time holds the silver chloride in solution. After standing one hour in the dark the gelatinoid precipitate is filtered and carefully washed until free of silver and nearly free of chlorides. It is then washed into a beaker, a few drops of HCl added, and after standing a few moments the silver is precipitated by leading a stream of H_2S through the solu-

Period II. The diet of sweetbreads. I ate three times daily one pair of sweetbreads (the thymus and the pancreas of the calf), which varied from 500 to 550 g. for the day. No other animal proteid was eaten, but bread and non-proteid vegetables were taken as in a normal diet; the diet contained about 120 g. of proteid and over 2400 calories of heat. The results are as follows:

Day	Urine.	Total N.	Urea N.	Per ct.	Urea.	Uric acid.	Bases.	$\overset{+}{\mathrm{U}}$. : $\overline{\mathrm{U}}$.	$\overline{\mathrm{U}}$. : B.	Total N.: Purin N.
1	1340 c.c.	20.944	17.920	85.5	38.400	1.413	0.0154	27.1 : 1	86.1 : 1	44 : 1
2	1900 "	29.702	20.454	68.8	43.830	1.540	0.0302	28.4 : 1	50.9 : 1	56.8 : 1
3	1510 "	19.404	17.832	91.8	38.212	0.412	0.0208	92.7 : 1	19.8 : 1	135.7 : 1
4	1250 "	18.816	16.800	89.2	36.000	0.554	0.0293	65 : 1	18.8 : 1	92.2 : 1
5	1220 "	Spoiled	17.360	...	37.200	0.374	0.0287	99.7 : 1	13 : 1	
6	1260 "	18.842	16.081	85.3	34.459	0.937	0.0384	36.7 : 1	24.4 : 1	57.5 : 1
Totals		107.708 129.249[1]	106.447	...	228.101	5.230	0.1628			
Averages		21.541	17.741	82.3	38.017	0.871	0.0271	32.1 : 1	31.9 : 1	72.1 : 1

On the third day of the period diarrhœa set in and continued for three days, accompanied by anorexia, nausea, headache, malaise, and some abdominal pain. The diet was continued unchanged and no drugs were taken. During these three days the quantity of uric acid fell to less than one-third of what it was the first days. On the last day the gastro-intestinal disturbances quieted and a large quantity of uric acid was eliminated. Judging from what we know of the metabolism of nuclein-rich foods, the figures of the first two days represent what the actual effects of such a diet are. The bases were not appreciably altered. What was the explanation of the fall in the uric acid? It was not due to lack of absorption and assimilation of the sweetbreads, since the total urinary nitrogen was maintained. That it was due to a retention there is no evidence. Either the uric acid was transformed into some other substance, possibly urea, or it was eliminated by the bowel; it was not possible to determine which. No albumin or sugar were present in the urine. The symptoms closely resembled those noted in experimental adenin poisoning.

Upon this diet the urine could not hold its uric acid in solution even at the body temperature. Obviously the current use of sweetbreads during convalescence from acute gout as a "light white meat" is not founded upon a knowledge of its properties. Three pounds were lost during this period, probably largely water.

Period III. A heavily proteid diet. In addition to some bread, fruits, green vegetables, and non-proteid desserts, I ate for breakfast six eggs, for luncheon and dinner each a sirloin beefsteak, and at midnight a large portion of cold roast-beef; these contained in all about 200 g. of proteid; the diet contained over 2500 calories. The results were as follows:

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[1] Calculated for the last day from the average.

Day	Urine.	Total N.	Urea N.	Per ct.	Urea.	Uric acid.	Bases.	$\overset{+}{U}$. : $\bar{U}$.	$\bar{U}$. : B.	Total N.: Purin N.
1	1520 c.c.	30.244	28.224	93.3	60.480	0.492	0.0091	122.9 : 1	46.3 : 1	182.1 : 1
2	1380 "	29.380	21.592	73.5	46.267	0.307	0.0329	150.7 : 1	9.3 : 1	277.1 : 1
3	1260 "	29.410	28.252	96.0	60.540	0.351	0.0238	172.4 : 1	14.7 : 1	237.1 : 1
4	1520 "	30.324	26.656	87.9	57.120	0.462	0.0289	123.6 : 1	16 : 1	185.4 : 1
5	1840 "	32.802	30.996	94.5	66.420	0.414	0.0201	160.4 : 1	20.6 : 1	227.7 : 1
6	1930 "	31.240	29.540	94.5	63.300	0.713	0.0193	88.7 : 1	36.9 : 1	149.4 : 1
Totals		183.400	165.260	...	354.127	2.739	0.1341			
Averages		30.566	27.543	90.1	59.021	0.456	0.0223	129.3 : 1	20.4 : 1	192.4 : 1

The diet agreed perfectly, and three pounds were gained in weight. The average urinary nitrogen, over 30 g., is an index of the excess of proteid in the diet, and likewise illustrates the Pflueger law of the assimilability of proteids. It is often stated that five pounds of meat per day may be easily eaten, and that some Indians can eat ten pounds in a day I know; for myself, however, the quantity in the above diet is the maximum. No albumin or sugar were in the urine.

Period IV. A purely vegetable diet, which contained no milk or eggs, nor was any animal fat used in the process of cooking. Incidentally remarked, it is the eggs, milk, and animal fats which are the salvation of so-called vegetarians; without them the diet is very bulky and also revolting. Naturally, a large quantity of pease and beans are required, to provide the necessary proteid, and they were both eaten, with large quantities of bread, three times daily, together with many other vegetables and nuts. The results were as follows:

Day	Urine.	Total N.	Urea N.	Per ct.	Urea.	Uric acid.	Bases.	$\overset{+}{U}$. : $\bar{U}$.	$\bar{U}$. : B.	Total N.: Purin N.
1	1080 c.c.	11.956	10.976	91.8	23.520	0.509	0.0165	46.2 : 1	30.8 : 1	68.7 : 1
2	1140 "	11.802	10.968	92.9	23.502	0.402	0.0157	58.4 : 1	25.6 : 1	84.9 : 1
3	1340 "	12.264	11.312	92.2	24.240	0.343	0.0230	70.6 : 1	14.9 : 1	101.3 : 1
4	1610 "	12.236	11.352	92.9	24.325	0.579	0.0256	42 : 1	22.6 : 1	60.8 : 1
5	980 "	11.382	10.248	90.0	21.960	0.501	0.0215	43.5 : 1	23.4 : 1	65.4 : 1
6	990 "	11.606	10.752	92.6	23.040	0.434	0.0148	53 : 1	29.2 : 1	77.8 : 1
Totals		71.246	65.608	...	140.587	2.771	0.1171			
Averages		11.874	10.934	92.0	23.430	0.462	0.0195	50.7 : 1	23.6 : 1	74.2 : 1

The ingestion of the maximum quantity of vegetables was not sufficient to furnish more than 12 g. of urinary nitrogen, which would correspond to about 90 g. of proteid in the diet. That this is sufficient for the needs of a body of this weight is accounted for by the fact that the diet contained an excess of carbohydrates, representing over 3000 calories, and we know that an excess of carbohydrates enables a body to economize upon its proteid metabolism. The body-weight was constant. The cooled urine at 20° C. precipitated no uric acid, which was in marked contrast to the precipitation noted in the other diets. No albumin or sugar were excreted.

PERIOD V. A milk diet. The milk was a modified milk obtained from the Walker-Gordon laboratory; 2750 c.c. were taken daily; it contained a little over 4 per cent. of proteids, 120 g. of proteids, and 6 per cent. each of sugar and fats, thus corresponding to about 2700 calories. The results were as follows:

Day	Urine.	Total N.	Urea N.	Per ct.	Urea.	Uric acid.	Bases.	$\overset{+}{\mathrm{U}}$. : $\overline{\mathrm{U}}$.	$\overline{\mathrm{U}}$. : B.	Total N.: Purin N.
1	1845 c.c.	17.668	16.660	91.1	35.700	0.289	0.0088	123.5 : 1	32.8 : 1	177.1 : 1
2	1105 "	18.421	17.792	96.5	38.125	0.250	0.0109	152.4 : 1	22.9 : 1	211.7 : 1
3	1260 "	17.724	16.408	92.5	35.160	0.236	0.0115	149 : 1	20.5 : 1	216.4 : 1
4	1210 "	18.862	17.920	95.0	38.400	0.308	Lost	124.6 : 1		
5	1330 "	17.808	16.432	92.2	35.211	0.293	0.0114	120.1 : 1	25.7 : 1	176.3 : 1
6	1110 "	17.042	16.184	91.9	34.680	0.329	0.0135	105.4 : 1	24.3 : 1	152.1 : 1
Totals[1]		107.528	101.396	...	217.276	1.705	0.0561 [1]0.0673			
Averages		17.921	16.899	91.3	36.213	0.284	0.0112	127.5 : 1	25.3 : 1	182.6 : 1

This diet agreed perfectly in every particular. At no time was uric acid precipitated from the urine cooled to 20° C. No albumin or sugar were present in the urine.

PERIOD VI. A nitrogen-free diet. Such a diet was composed of 350 g. of pure sago, 50 g. of sugar, and 100 g. of butter per day. The sago was a manufactured product, and contained on analysis but 0.069 g. of nitogren in the daily ration. The butter contained, on an average of four analyses, 0.125 g. of nitrogen in the daily ration; the sugar contained none; thus the entire daily ration of carbonous food contained less than 0.200 g. of nitrogen; it represented over 2500 calories. This diet was fully sufficient to supply the heat of the body, but for its nitrogenous metabolism the body was thrown entirely upon its own tissues; it was to determine the actual nucleinic output under such conditions that the diet was undertaken. The results were as follows:

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[1] Calculated for the last day from the average.

Day	Urine.	Total N.	Urea N.	Per ct.	Urea.	Uric acid.	Bases.	$\overset{+}{U}$. : $\overline{U}$.	$\overline{U}$. : B.	Total N.: Purin N.
1	1810 c.c.	5.432	4.116	75.7	8.820	0.307	0.0065	28.7 : 1	47.2 : 1	52.2 : 1
2	1510 "	4.578	3.916	85.5	8.391	0.401	0.0050	20.7 : 1	80.2 : 1	33.9 : 1
3	1440 "	4.102	3.560	86.7	7.627	0.241	0.0060	31.2 : 1	40.1 : 1	50 : 1
4	1560 "	4.162	3.552	85.3	7.611	0.271	0.0081	28 : 1	38.4 : 1	44.7 : 1
5	1300 "	4.228	3.276	77.4	7.020	0.227	0.0076	30.9 : 1	30 : 1	56.3 . 1
6	1310 "	3.780	3.248	85.9	6.960	0.189	0.0068	36.8 : 1	27 : 8	58.1 : 1
Totals		26.282	21.668	...	46.429	1.636	0.0400			
Averages		4.380	3.611	82.4	7.738	0.273	0.0066	28.3 : 1	41.3 : 1	47.1 : 1

About six pounds were lost during this period of eight days, during which the bowels moved but twice. The diet caused very little digestive disturbance, but toward the close of the experiment there was a distinct loss of strength. Neither sugar nor albumin appeared in the urine, which was almost colorless, and held all its uric acid in solution when cooled to 20° C.

This experiment shows how the body will economize in its nitrogenous metabolism. In the various studies of the urine during starvation the output of urinary nitrogen has usually been double that present in this experiment; obviously the carbonous food shielded the tissues to that extent. While the diet cannot be called a physiological one, the figures probably represent the minimum nitrogenous metabolism. When we compare the figures here obtained with those afforded by the heavily proteid diet, where *seven* times as much urinary nitrogen was eliminated, we perceive the wide latitude of adaptability which our nitrogenous metabolism possesses, and which is in such marked contrast to the limited range of the carbonous metabolism.

Following the period of nitrogen-free diet a long rest was taken, and the next experiment was not begun until the body had recovered the lost weight. In this period (VII.) a normal diet was taken, the same as in the first period, but with the addition of three cups of coffee per day—one large cup at breakfast and a small cup of *café noir* at luncheon and dinner. Two bottles of beer were taken daily, about 0.700 l. The results were as follows:

Day	Urine.	Total N.	Urea N.	Per ct.	Urea.	Uric acid.	Bases.	$\overset{+}{\mathrm{U}}.:\overline{\mathrm{U}}.$	$\overline{\mathrm{U}}.:\mathrm{B}.$	Total N.: Purin N.
1	2515 c.c.	16.908	15.682	92.7	33.604	0.703	0.0506	47.8 : 1	13.9 : 1	67.9 : 1
2	1280 "	19.908	18.312	91.9	39.240	0.793	0.0461	49.3 : 1	17.2 : 1	71.6 : 1
3	2220 "	22.284	18.396	82.5	39.420	0.666	0.0555	59.2 : 1	12 : 1	93.2 : 1
4	1560 "	22.144	19.696	88.9	42.205	0.790	0.0530	53.4 : 1	14.9 : 1	79.3 : 1
5	1290 "	22.372	20.216	90.3	43.320	0.808	0.0556	53.6 : 1	14.5 : 1	78.2 : 1
6	1280 "	21.168	19.516	92.1	41.820	0.568	0.0656	71.8 : 1	8.6 : 1	101.2 : 1
Totals		124.784	111.818	...	239.609	4.328	0.3264			
Averages		20.797	18.636	89.6	39.935	0.721	0.0544	55.4 : 1	13.2 : 1	80.9 : 1

The striking increase in the uric acid and bases is the only thing noted in the results. Since both beer and coffee entered into the diet, another period (VIII.) was carried through, in which, with the same diet and a little more coffee, no alcoholic beverage was taken. The results were as follows:

Day	Urine	Total N.	Urea N.	Per ct.	Urea.	Uric acid.	Bases.	$\overset{+}{\mathrm{U}}.:\overline{\mathrm{U}}.$	$\overline{\mathrm{U}}.:\mathrm{B}.$	Total N.: Purin N.
1	1590 c.c.	18.480	16.576	89.6	35.520	0.942	0.0721	37.4 : 1	13 : 1	55 : 1
2	1100 "	18.352	17.296	94.2	37.062	0.953	0.0515	38.9 : 1	18.5 : 1	55.6 : 1
3	2100 "	19.012	17.612	92.6	37.740	0.821	0.0791	45.9 : 1	10.3 : 1	63.3 : 1
4	1610 "	21.840	19.516	89.2	41.820	0.657	0.0622	63.6 : 1	10.5 : 1	91.7 : 1
5	1325 "	22.176	20.095	90.6	43.060	0.821	0.0683	52.4 : 1	12 : 1	76.1 : 1
6	1860 "	20.396	18.732	91.9	40.182	0.765	0.0578	52.9 : 1	13.2 : 1	74.9 : 1
Totals		120.256	109.827	...	235.384	4.959	0.391			
Averages		20.043	18.304	91.3	39.225	0.826	0.0651	47.4 : 1	12.6 : 1	68 : 1

The following table contains a comparative summary of the average results:

Diet..	Total N.	Urea N.	Per ct.	Urea.	Uric acid.	Bases.	$\overset{+}{U} : \bar{U}$.	$\bar{U}$. : B.	Total N.: Purin N.
Normal	20.936	19.018	90.8	40.752	0.364	0.0249	112 : 1	14.6 : 1	162.9 : 1
Sweetbread	21.541	17.741	82.3	38.017	0.871	0.0271	43.6 : 1	32.1 : 1	72.1 : 1
Heavy proteid	30.566	27.543	90.1	59.021	0.456	0.0223	129.3 : 1	20.4 : 1	192.4 : 1
Vegetable	11.874	10.943	92.0	23.430	0.462	0.0195	50.7 : 1	23.6 : 1	74.2 : 1
Milk	17.921	16.899	94.3	36.213	0.284	0.0112	127.5 : 1	25.3 : 1	182.6 : 1
Carbonous	4.380	3.611	82.4	7.738	0.273	0.0066	28.3 : 1	41.3 : 1	47.1 : 1
Normal, with coffee and beer	20.797	18.636	89.6	39.935	0.721	0.0544	55.4 : 1	13.2 : 1	80.9 : 1
Normal, with coffee alone	20.043	18.304	91.3	39.225	0.826	0.0651	47.4 : 1	12.6 : 1	68 : 1

SUMMARY OF RESULTS. In all the experiments, except in VI., the total urinary elimination of nitrogen corresponds with the input. This nitrogen represents the common proteid metabolism of the body, and has absolutely no constant relations to the nucleinic metabolism. This is a fact of fundamental importance. The common nitrogenous metabolism is a process of low specialization, and produces a large amount of output in the form of urea and ammonia. The nucleinic metabolism is a highly specialized process which produces a small output of uric acid and purin bases. When these distinctions are clearly understood, when we realize that each of these may be increased or decreased independent of the other, when we perceive their factive independence, we will understand how worthless are the ratios based upon a comparison of their results, as the urea-uric acid ratio. I will return to this point.

The figures for urea are very interesting, inasmuch as they differ notably from the figures commonly observed in diet experiments. The urea constitutes in my case a much higher percentage of the total nitrogen than is usual. Upon the normal diet of the first period the average was 90.8 per cent.; it fell to 82.3 per cent. upon the abnormal sweetbread diet; upon the heavily proteid diet it was 90.1 per cent.; upon the vegetable diet, 92 per cent.; it rose to 94.3 per cent. upon the milk diet, fell to 82.4 per cent upon the carbonous diet, and upon the two last diets was respectively 89.6 per cent. and 91.3 per cent. The average for the physiological diets was, therefore, 91.3 per cent. of the total nitrogen, which is about 5 per cent. above the figures usually seen. A partial explanation may lie in the fact that the total nitrogen was more than usual; in most of the work from 16 to 17 g. of nitrogen constituted the output; here the average in the physiological diets was over 20 g.; since the difference is most largely in the urea, this might explain the higher percentage. The fact, however, that the highest figure was seen in the milk diet—94.3 per cent.—and not in the heavily proteid diet—90.1 per cent.—excludes such an explanation. The cause must lie in an individual peculiarity of metabolism; there was more urea and less ammonia and kreatinin eliminated simply because that was the habitus of the individual metabolism.

The uric acid was lowest, during the periods of a natural diet, upon the milk diet, the average being 0.284 g. per diem. It was very little less upon the carbonous diet—0.273 g.—so that these figures may be taken to represent the actual extent of essential nucleinic metabolism. Upon a normal diet (I.) the uric acid was 0.364 g. This increase over a milk diet may be conceived as the result either of the ingestion in the diet of nucleins which appear as uric acid, or of a stimulation of the nucleinic metabolism by something in the diet; the first explanation seems to-day the more probable. Upon a heavily proteid diet the uric acid rose to 0.456 g., nearly a hundred milligrammes over the quantity from a diet similar, except for the excess of proteid. Upon a purely vegetable diet the uric acid was still a little higher than upon the heavily proteid diet, 0.462 g. When we consider that in a vegetable diet we are compelled to include a large quantity of seeds (pease and beans and nuts), in order to procure the necessary proteid, and that these seeds are rich in nucleins, the high figures for uric acid are only the natural and expected results.

The average, 0.871 g., for the sweetbread diet is misleading, on account of the complication of diarrhoea during the third, fourth, and fifth days. An average of the other three days, 1 260 g., represents the output more accurately. The excess is due to the large quantity of nucleins in sweetbreads, which are eliminated as uric acid.

When coffee and beer were added to a normal diet (VII.) the uric acid rose to 0.721 g.—just double the figure seen upon a normal diet without coffee and beer (I.). This excess was probably due entirely to the fact that the nucleins in coffee and beer are eliminated in part as uric acid. Caffeine is, as we know, a purin base, and we would expect it to increase the purin bodies in the urine. In order to eliminate the factor of the beer, this was excluded in diet VIII. and a little more coffee added; the uric acid rose still higher—to 0.826 g. per diem. Apparently the beer had little influence. It is therefore apparent that in connection with the use of coffee the elimination of uric acid may be more than doubled, and that in ordinary life more than half of our uric acid may come not from our food, nor from our tissues, but from our beverages. That fact, of course, does not show in the least that those beverages are bad; it must be first shown that the uric acid which results from them is harmful.

The failure of a heavy meat diet to exaggerate the elimination of uric acid is contrary to the time-honored English theories, and yet it is what a careful consideration would lead us to expect. Muscular tissue is not rich in nucleins, and, so far as we know, it is only from nucleins and purin compounds in the diet that uric acid can be derived dietetically. The output of uric acid upon the vegetable diet is, of course, a heretical performance, but nevertheless one in direct harmony with the nucleinic richness of the pease and beans which must form so large a part of a vegetable diet.

These figures demonstrate again the comparative (and for clinical purposes, complete) worthlessness of the urea-uric acid ratio, the sacred $\overset{+}{U} : \overline{U}$ of our books. Upon a normal diet (I.) it was 112.1. Upon a sweetbread diet, where the uric acid was much increased and the urea but little affected, it was 43.6 : 1. Upon the heavily proteid diet the urea was much increased and the uric acid but little, so the ratio rose to 129.3 : 1. Upon the vegetable diet, where the uric acid was somewhat increased and the urea markedly diminished, the ratio was 50.7 : 1. Upon the milk diet, where the uric acid was low and the urea high, it was 127.5 : 1—almost identical with the ratio seen in the heavily proteid diet. Upon the nitrogen-free diet (VI.) both the uric acid and the urea were low, the latter, however, much the most, and the ratio was 28.3 : 1. This was the only experiment in which I reached the gout-ratio of Haig. In these experiments the more proteid eaten the further from the gout-ratio was the $\overset{+}{U} : \overline{U}$; when no proteid was eaten the gout-ratio was attained. The ratios during the last two periods with coffee, 55.4 : 1 and 47.4 : 1, are about the normal figures usually quoted. When they are contrasted with those seen upon a normal diet, 112.1, the striking results of the coffee are seen. In view of the wide currency of Haig's views, it seems necessary to emphasize the necessary conclusions from these figures. Since we know that the urea is influenced largely by the quantity of proteid in the diet and by the proteid metabolism; that the plain proteid has little influence upon the nucleinic metabolism or the elimination of the purin compounds; and that the nucleinic metabolism and the substances which affect it, and the elimination of the purin bodies, have little effect upon the urea formation, it must follow that the urea-uric acid ratio is almost valueless, and, as a basis of pathological reasoning as it is employed in current clinical medicine, entirely worthless.

The average amount of purin bases eliminated upon a normal diet (I.) was 0.0249 g. During the sweetbread diet (II.) there was but little change, the average being 0.0271 g., a slight increase, but one of no moment. Apparently all the nucleins in this diet passed into uric acid. Upon a heavily proteid diet (III.) the average figure was 0.0223 g. per day, a slight reduction below the average of the first period, but one too small to be of any importance. Upon the vegetable diet (IV.) the average of bases fell still lower—0.0195 g.—though only to a slight